Original Article

# Positivity Rates of Histology Results Based on Lesion Size and Bronchus Sign in Lung Cancer

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**Submitted:** March 6th, 2025
**Accepted:** April 22nd, 2025
**Published:** June 13th, 2025

**Respir Sci. 2025; 5(3): 176-84**
https://doi.org/10.36497/respirsci.v5i3.175



## Abstract

**Background:** Lung cancer continues to be a major cause of cancer-related deaths globally. Bronchoscopy serves as a key diagnostic tool, allowing histological sampling through transbronchial biopsy (TBB). The bronchus sign, identified on pre-biopsy CT scans, is associated with improved diagnostic yield in TBB.

**Method:** A retrospective study was conducted between October and December 2023 at Persahabatan Hospital, Jakarta, analyzing 88 patients suspected of lung cancer. Data collected comprised patient demographics, lesion size as determined by CT scans, and the presence or absence of the bronchus sign. Fisher's exact test was applied for statistical analysis, with a predetermined significance level of $P<0.05$.

**Results:** Positive histology results were identified in 38 cases (55.07%) for lesions ≥3 cm and 9 cases (47.39%) for <3 cm($P=0.607$). In lesions ≥3 cm, the positivity rate was similar between those with the presence (55.81%) and absence (53.85%) of a bronchus sign ($P>0.99$). In lesions <3 cm, positivity was higher with a bronchus sign (60%) than without (25%) ($P=0.55$).

**Conclusion:** The bronchus sign appears to increase TBB positivity, especially in peripheral lesions <3 cm. Lesion size also appears to influence TBB yield. However, the findings were not statistically significant, likely due to small sample size and missing CT data.

**Keywords:** bronchoscopy, bronchus sign, lung cancer, transbronchial biopsy

## INTRODUCTION

Lung cancer remains a leading malignancy and cause of cancer-related deaths in Indonesia and worldwide. According to Global Cancer Statistics 2022, lung cancer was the most diagnosed cancer, with 2.5 million new cases, accounting for 12.4% of all newly reported cancers. It also remained the leading cause of cancer-related deaths, contributing to

1.8 million fatalities (18.7% of total cancer deaths).[1,2]

Early detection and surgery are key to improving survival, with a five-year survival rate of 66-82% in early-stage non-small cell lung cancer (NSCLC).[3,4] Imaging plays a key role in early detection, with chest X-rays identifying nodules as small as 0.5-1 cm, while CT scans provide clearer detail of lesion size and location.[5,6]

Bronchoscopy is a primary diagnostic tool for suspected lung cancer, enabling tissue sampling through transbronchial biopsy (TBB), transbronchial needle aspiration (TBNA), airway electrosurgery, or cryotherapy.[7] Factors affecting diagnostic yield include lesion size, location, and bronchus sign, which indicates whether a bronchus leads directly to the lesion on a pre-biopsy CT scan.[8]

The bronchus sign indicates the presence of bronchi within the target identified on the pre-biopsy thoracic CT scan.[9] However, if the bronchus sign remains unclear, it may be prudent to consider bronchoscopy with TBB as a diagnostic modality, as the positive yield is often low in the absence of additional diagnostic tools.[10] Several studies indicate that diagnostic outcomes are influenced by target lesion characteristics, including size, proximity to the hilum, and the bronchus sign.[11]

Tsuboi's classification categorizes tumor-bronchus relationships to guide TBB. Type I: patent bronchus leading to the tumor; Type II: bronchus within the tumor; Type III: compressed bronchus; Type IV: severely narrowed proximal bronchus.[12,13]

Since the Tsuboi classification cannot be fully applied to the relationship of the bronchi to peripheral lesions on CT, the subclassification of the CT-bronchus sign (CT-BS), which is more practical, is proposed. Ultimately, this classification was simplified into two categories: positive and negative CT-BS. This subclassification is highlighted as a practical and effective guiding method, as it enhances diagnostic success by enabling lesion access with minimal additional equipment, such as fluoroscopy.[11,14,15]

Transbronchial biopsy is a technique for sampling lung parenchyma using forceps through the distal tip of a flexible bronchoscope. TBB is recommended for suspected lung cancer, with a sensitivity of approximately 85% for endobronchial lesions, 60-70% for peripheral lesions, and 56% for nodules <20 mm.[3,16,17] Diagnostic yield for lesions <3 cm varies from 14-50%, compared to 46-80% for lesions ≥3 cm. Fluoroscopy improves TBB accuracy but requires expertise.[18,19]

Transbronchial biopsy samples can be acquired using various techniques, including fluoroscopy guidance, CT navigation, radial-probe endobronchial ultrasound, bronchial mapping, augmented fluoroscopy, cone beam-CT, robotic-assisted bronchoscopy, or electromagnetic navigation.[20,21] Diagnostic yield increases with more biopsy samples. Positive TBB results reach 70%, improving further with combined bronchial brushing and TBNA.[22,23]

Previous studies have shown that small peripheral pulmonary lesions (PPLs)

invisible under fluoroscopy can be accurately located using a three-dimensional localization technique on the chest wall surface, allowing bronchoscopy procedures to increase diagnostic yields.[24] Other factors influencing the diagnostic yield include lesion size, its proximity to the hilum (with higher yield observed in lesions closer to the hilum), visibility on fluoroscopy, malignancy status, and the combination of diagnostic tools used.

Meanwhile, determining whether a lesion is small or large is not the same between one study and another. Sanchez-Font et al, for example, used a cutoff of <30 mm, while Boonsarngsuk et al and Ishid et al used a cutoff of <20 mm.[25] Fluoroscopy in TBB for focus can improve diagnostic results by helping to determine the target area more accurately.[26]

## METHOD

This retrospective study was conducted from October to December 2023 at Persahabatan Central General Hospital, East Jakarta, using medical records. Ethical clearance was obtained before the study. All procedures were carried out in line with the ethical principles of the Declaration of Helsinki. After informed consent, fluoroscopy-guided TBB was performed on 88 patients with suspected peripheral lung cancer.

All patients underwent a Thoracic CT scan with contrast before image-guided bronchoscopy with fluoroscopy guidance. Bronchoscopic instruments included Olympus Exera 3 and Fujinon 7700. Anatomical pathology diagnosis was performed by a specialist at Persahabatan Hospital.

After localizing the lesion with fluoroscopy, forceps were inserted to reach the target. Once positioned, the forceps were opened and advanced into the lesion. A minimum of 4–5 specimens were obtained for analysis.

## RESULT

This study included 88 patients with suspected peripheral lung cancer at Persahabatan Hospital, East Jakarta, from October to December 2023. The study included 59 males and 29 females, with 71 participants aged ≥40 years and 17 <40 years. Bronchus signs were present in 53 CT scans, absent in 17, and missing in 18, which were excluded. The characteristics of the patients are presented in Table 1.

Table 1. Patient characteristics (n=88)

| Variable | n (%) |
|---|---|
| Age (mean) | |
| <40 | 17 (19.1%) |
| ≥ 40 | 71 (79.8%) |
| Gender | |
| Male | 59 (66.3%) |
| Female | 29 (32.6%) |
| Lesion size | |
| <3cm | 19 (21.3%) |
| ≥3cm | 69 (77.5%) |
| Bronchus Sign | |
| Presence | 53 (59.6%) |
| Absence | 17 (19.1%) |
| Exclude | 18 (20.2%) |

In this study, the pathology results were compared between two groups based on lesion size: ≥3 cm and <3 cm. Table 2 presents the distribution of histology

results for each group. Among lesions ≥3 cm, 38 cases (55.07%) were positive; in lesions <3 cm, 9 cases (47.39%) were positive.

Fisher's exact test was conducted to determine the significance of these discrepancies with results were not statistically significant (P=0.607), the odds ratio was found to be 1.39 with a 95% confidence interval (CI) of 0.53–3.77, indicating a tendency for higher odds of positive pathology results in the ≥3 cm group compared to the <3 cm group.

This study also evaluated the histology results between the two groups based on the presence and absence of bronchial indications. Table 2 presents the distribution of histology results in each group. In lesions ≥3 cm with a bronchus sign, 24 cases (55.81%) were positive, while in the group without a bronchial sign, 7 cases (53.85%) had a positive histological outcome.

Fisher's exact test was done to determine the significance of these differences, and the results show that the odds ratio was obtained at 1.083 with 95% CI=0.31-3.77), indicating no significant difference between groups with and without a bronchus sign, but this result is not statistically significant (P>0.99). The findings are further illustrated in Table 2, which visually represents the percentage of each tumor size group's positive histology findings.

In this study, histology results were compared between two groups based on the presence or absence of a bronchus sign in lesions <3 cm. Table 2 presents the distribution of pathology results in each group. In the group with the bronchus sign, six cases (60%) had positive histology results, while only 1 case (25%) was positive in the group without a bronchus sign.

Fisher's exact test was performed to determine the significance of these differences and the results was not statistically significant (P=0.55), the odds ratio was 4.5 with a 95% CI=0.45–66.62, which showed a tendency for a higher chance of positive histology results in the group with bronchus signs compared to the group without bronchus signs. Table 2 shows the proportion of positive histology results by bronchus sign in <3 cm lesions.

Table 2. Proportion of positive histology results based on lesion size, bronchus sign in group size ≥3cm, and Bronchus sign in group size <3cm

| Group | Positive | Negative | P | OR (95% CI) |
|---|---|---|---|---|
| Lesion size | | | | |
| <3cm | 9 (47.37%) | 10 (52.63%) | 0.607* | 1.39 (0.53–3.77) |
| ≥3cm | 38 (55.07%) | 31 (44.92%) | | |
| Bronchus sign in group size ≥3cm | | | | |
| Presence | 24 (55.81%) | 19 (44.19%) | >0.99 | 1.083 (0.31-3.77) |
| Absence | 7 (53.85%) | 6 (46.15%) | | |
| Bronchus sign in group size <3cm | | | | |
| Presence | 6 (60.00%) | 4 (40.00%) | 0.55 | 4.5 (0.45–66.62) |
| Absence | 1 (25.00%) | 3 (75.00%) | | |

Note: *Fisher's exact test with P>0.05 not significant; OR=odds ratio

## DISCUSSION

The study involved patients with suspected lung cancer at Persahabatan General Hospital, East Jakarta, from October to December 2023. The sample was 88 people, with patients >40 years old (79.8%). The majority of patients were males (66.3%) with a tumor size generally ≥3 cm (77.5%) at the time of diagnosis. Of the 88 patients, only 70 had evaluable CT scans for bronchus signs, with 59% of them having a bronchial sign image on the CT scan. There are 18 patients whose bronchus sign image could not be analyzed because there were no CT results in the electronic medical record, so they were removed from the analysis.

Ermayanti et al reported that men have a higher likelihood of developing lung cancer than women, with an incidence rate of 77.8% in men. The trend of lung cancer incidence in both sexes has fluctuated over the years. Additionally, multiple studies indicate that the 5-year survival rate is higher in women than in men.[26] Smoking, second-hand smoke, radon gas, asbestos, carcinogens, air pollution, and aging are risk factors for lung cancer. The higher incidence in men is mainly linked to smoking history.[27,28]

The incidence of lung cancer is highly age-related, with the highest rate among older people.[29] The age-based incidence increased sharply in the 45-49 years age group and decreased in the older age group. The highest incidence was in the 75-79 year age group for women and the 85-89 year old group for men. This aligns with our study, which also showed a significantly higher number of cases in individuals over 40 years old.[30]

In this study, we compared positive external histological results between groups of lesions measuring ≥3 cm and <3 cm based on CT scans performed by TBB bronchoscopy. There was no statistically significant difference in positive TBB results between the two groups, although the group of lesions with size ≥3 cm had a tendency to have a higher level of positivity when compared to the size lesions<3cm (OR=1.39; 95% CI=0.5364-3.779). However, this result is also not statistically significant (P>0.05) due to the small sample size and incomplete CT scan data in medical records.

Labbé et al, in their study, performed bronchoscopy with bronchial aspiration, brushing, and bronchoalveolar lavage (BAL) and found that the overall diagnostic yield increased with lesion size, reaching its peak at a diameter of 3 cm. Beyond this threshold, further increases in lesion size did not significantly enhance diagnostic performance.[31] Several recent technologies for guiding TBB, such as CT navigation, radial EBUS, electromagnetic navigation, robotic-assisted bronchoscopy, augmented fluoroscopy, and cone beam CT, have improved the positivity rates in sampling peripheral lung lesions.[22]

To assess the role of the bronchus sign regarding the positivity rate of TBB results, we divided the analysis into two separate groups: lesions ≥3 cm and lesions <3 cm. In the group of lesions ≥3 cm, the presence or absence of a bronchus

sign did not affect the positivity rate (OR=1.083; 95% CI=0.32–3.77; P=0.99). On the other hand, although not statistically significant (P=0.55), the presence of a bronchus sign in the group of lesions <3 cm showed a tendency to increase the positivity of TBB results (OR=4.5; 95% CI=0.45–66.62).

The size of the lesion influences the diagnostic yield, as does its visibility on fluoroscopy and the combination of diagnostic tools used. However, the criteria for classifying a lesion as small or large can vary between studies, which may affect the results. For example, Tateishi et al used 30 mm as the cutoff for tumor size, with a median size of 38 mm. Similarly, Sanchez-Font et al also applied a <30 mm threshold, whereas Boonsarngsuk et al and Ishid et al classified tumors as small when they were <20 mm.[25,32] Fluoroscopy in TBB can enhance diagnostic results by helping to more accurately determine the target area.[25]

The CT-BS has been shown to improve the diagnostic yield of peripheral lung lesions.[15] However, the clinical significance of the CT-BS remains controversial. Multiple studies suggest that the outcomes are affected by target lesion characteristics, including size, proximity to the hilum, and the presence of the CT-BS.[11] Ng et al reported that fluoroscopy-guided TBB achieved a diagnostic yield of approximately 83.4%, with a low overall complication rate, including pneumothorax. They emphasized the importance of adequate planning and preparation to minimize the risk of pneumothorax.[33]

Ost et al reported that TBB of peripheral lesions was diagnostic in 43.2% of cases. They also found that the overall diagnostic yield of bronchoscopy was 53.7%, with a sensitivity for lung cancer ranging from 60% to 74%. Additionally, they noted that the specimens obtained were usually adequate for diagnosing adenocarcinoma in 38.5% of patients.[34] The target location is not always visible on fluoroscopy and cannot always be precisely identified using fluoroscopy-guided bronchoscopy techniques, which can affect the diagnostic results.[35,36]

## CONCLUSION

The bronchus sign may increase TBB positivity, especially in peripheral lesions <3 cm. The size of the lesion also tends to influence the positivity rate of TBB. Larger lesions are generally associated with higher diagnostic yields. However, small sample size and missing CT data limited statistical significance.

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